neuropathy, ataxia, and retinitis pigmentosa

Neuropathy, ataxia, and retinitis pigmentosa (NARP) is a condition that causes a variety of signs and symptoms chiefly affecting the nervous system. Beginning in childhood or early adulthood, most people with NARP experience numbness, tingling, or pain in the arms and legs (sensory neuropathy); muscle weakness; and problems with balance and coordination (ataxia). Many affected individuals also have vision loss caused by changes in the light-sensitive tissue that lines the back of the eye (the retina). In some cases, the vision loss results from a condition called retinitis pigmentosa. This eye disease causes the light-sensing cells of the retina gradually to deteriorate.

Learning disabilities and developmental delays are often seen in children with NARP, and older individuals with this condition may experience a loss of intellectual function (dementia). Other features of NARP include seizures, hearing loss, and abnormalities of the electrical signals that control the heartbeat (cardiac conduction defects). These signs and symptoms vary among affected individuals.

Frequency

The prevalence of NARP is unknown. This disorder is probably less common than a similar but more severe condition, Leigh syndrome, which affects about 1 in 40,000 people.

Genetic Changes

NARP results from mutations in the *MT-ATP6* gene. This gene is contained in mitochondrial DNA, also known as mtDNA. Mitochondria are structures within cells that convert the energy from food into a form that cells can use. Although most DNA is packaged in chromosomes within the nucleus, mitochondria also have a small amount of their own DNA.

The *MT-ATP6* gene provides instructions for making a protein that is essential for normal mitochondrial function. Through a series of chemical reactions, mitochondria use oxygen and simple sugars to create adenosine triphosphate (ATP), the cell's main energy source. The MT-ATP6 protein forms one part (subunit) of an enzyme called ATP synthase, which is responsible for the last step in ATP production. Mutations in the *MT-ATP6* gene alter the structure or function of ATP synthase, reducing the ability of mitochondria to make ATP. It remains unclear how this disruption in mitochondrial energy production leads to muscle weakness, vision loss, and the other specific features of NARP.

Inheritance Pattern

This condition is inherited in a mitochondrial pattern, which is also known as maternal inheritance. This pattern of inheritance applies to genes contained in mtDNA. Because egg cells, but not sperm cells, contribute mitochondria to the developing embryo, children can only inherit disorders resulting from mtDNA mutations from their mother. These disorders can appear in every generation of a family and can affect both males and females, but fathers do not pass traits associated with changes in mtDNA to their children.

Most of the body's cells contain thousands of mitochondria, each with one or more copies of mtDNA. The severity of some mitochondrial disorders is associated with the percentage of mitochondria in each cell that has a particular genetic change. Most individuals with NARP have a specific *MT-ATP6* mutation in 70 percent to 90 percent of their mitochondria. When this mutation is present in a higher percentage of a person's mitochondria—greater than 90 percent to 95 percent—it causes a more severe condition known as maternally inherited Leigh syndrome. Because these two conditions result from the same genetic changes and can occur in different members of a single family, researchers believe that they may represent a spectrum of overlapping features instead of two distinct syndromes.

Other Names for This Condition

- NARP
- NARP syndrome
- neurogenic muscle weakness, ataxia, and retinitis pigmentosa
- neuropathy, ataxia, and retinitis pigmentos

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Neuropathy ataxia retinitis pigmentosa syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1838914/

Other Diagnosis and Management Resources

- GeneReview: Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224
- GeneReview: Mitochondrial DNA-Associated Leigh Syndrome and NARP
  https://www.ncbi.nlm.nih.gov/books/NBK1173
- MedlinePlus Encyclopedia: Retinitis pigmentosa
  https://medlineplus.gov/ency/article/001029.htm

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Retinitis pigmentosa
  https://medlineplus.gov/ency/article/001029.htm
- Health Topic: Cerebellar Disorders
  https://medlineplus.gov/cerebellardisorders.html
- Health Topic: Mitochondrial Diseases
  https://medlineplus.gov/mitochondrialdiseases.html
- Health Topic: Retinal Disorders
  https://medlineplus.gov/retinaldisorders.html

Genetic and Rare Diseases Information Center

- Neuropathy ataxia retinitis pigmentosa syndrome
  https://rarediseases.info.nih.gov/diseases/262/neuropathy-ataxia-retinitis-pigmentosa-syndrome

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke
  https://www.ninds.nih.gov/Disorders/All-Disorders/Mitochondrial-myopathy-Information-Page

Educational Resources

- Cleveland Clinic Health Information Center
  http://my.clevelandclinic.org/health/articles/myths-and-facts-about-mitochondrial-diseases
- Kennedy Krieger Institute
  https://www.kennedykrieger.org/patient-care/diagnoses-disorders/mitochondrial-disorders
- MalaCards: mitochondrial dna-associated leigh syndrome and narp
  http://www.malacards.org/card/mitochondr
  ial_dna_associated_leigh_syndrome_and_narp
- Neuromuscular Disease Center, Washington University
  http://neuromuscular.wustl.edu/mitosyn.html#narp
- Orphanet: NARP syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=644

Patient Support and Advocacy Resources

- Children's Mitochondrial Disease Network (UK)
  http://www.cmdn.org.uk/
- Foundation Fighting Blindness: Retinitis Pigmentosa
  http://www.blindness.org/retinitis-pigmentosa
- MitoAction
  http://www.mitoaction.org/
- Muscular Dystrophy Association: Facts About Mitochondrial Myopathies
  https://www.mda.org/sites/default/files/publications/Facts_MITO_P-216.pdf
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/maternally-inherited-leigh-syndrome-and-narp-syndrome/
- Resource list from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/mitochon.html
- United Mitochondrial Disease Foundation
  http://www.umdf.org/

GeneReviews

- Mitochondrial Disorders Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1224
- Mitochondrial DNA-Associated Leigh Syndrome and NARP
  https://www.ncbi.nlm.nih.gov/books/NBK1173

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22neuropathy%2C+ataxia%2C+and+retinitis+pigmentosa%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Mitochondrial+Diseases%5BMAJR%5D%29+AND+%28%28neuropathy,+ataxia,+and+retinitis+pigmentosa%5BTIAB%5D%29+OR+%28narp%5BTIAB%5D%29+OR+%28narp+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- NEUROPATHY, ATAXIA, AND RETINITIS PIGMENTOSA
  http://omim.org/entry/551500

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  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1722923/
- GeneReview: Mitochondrial DNA-Associated Leigh Syndrome and NARP
  https://www.ncbi.nlm.nih.gov/books/NBK1173
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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/9221962
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Reviewed: November 2006
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services